REMARKS

Claims 6-12, 38-45, 47, and 48 are active in the present application. Support for the amendment to Claim 48 is found on page 6, lines 18-20: "The lineage committed human cell used in accordance with the present invention are cells which are differentiated to at least a point where they are programmed to develop into a specific type of cell." In addition, support for the amendment to claim 48 is found in Claim 42 (prior to the current amendment) and Claim 47. No new matter is believed to have been added by these amendments.

The present invention provides a method for obtaining lineage committed cells, which are those cells that are differentiated to at least a point where they are programmed to develop into a specific type of cell, with enhanced biological function by culturing with a liquid medium replacement rate of at least 25% daily replacement for more than one day (see Claim 38). This method is not described in the prior art cited for the following reasons.

Emerson et al (U.S. Patent No. 5,437,994) describe culturing human bone marrow stromal cells by a method where a liquid culture medium is replaced or perfused at a specified rate (see col. 4, lines 39 through col. 5, line 9 and col. 7, lines 60-64). However, human bone marrow stromal cells are not lineage committed cells as defined in the present claims, i.e., "differentiated to at least a point where they are programmed to develop into a specific type of cell." Bone marrow stromal cells are known to be multipotent or cells that can develop into many different types of cells, i.e., progenitor or stem cells, which is supported by the general knowledge concerning bone marrow stromal cells (see Prockop DJ. Marrow stromal cells as stem cells for nonhematopoietic tissues. *Science* 1997 Apr 4;276(5309):71-4—a copy was provided to the Patent Office with the February 2003 filing).

In view of the above, Applicants request withdrawal of the rejection over Emerson et al.

Similarly, Caldwell et al describe culturing bone marrow stromal cells to detect GM-CSF secretion (see page 350, column 1). As noted above, bone marrow stromal cells are NOT lineage committed human cells as in the present claims. Therefore, the present claims cannot be anticipated by Caldwell et al and withdrawal of the rejection over Caldwell is requested.

Turning to the rejection over Freedman et al, Applicants point out that the method of Freedman et al involves culturing tumor infiltrating lymphocytes with the following steps: "The cultures were typically inspected every 3-4 days and fed by removing one half of the medium in the wells and replacing it with fresh complete AIM V medium." (See the paragraph bridging pages 147-148). The Freeman et al method also includes transferring cells to a flask that "were fed with fresh complete AIM V medium twice weekly" (page 148, col. 1, paragraph 1); adding fresh medium to maintain cell concentration where "[c]ell numbers and viability were determined every 3-4 days" (page 148, col. 1 paragraph 2); and then through a artificial capillary culture system to circulate the media for "oxygenation and gas exchange" (page 148, col. 1, paragraph 3).

However, Freedman et al do not describe the claimed method of culturing a lineage committed human hematopoietic cell composition which includes a liquid medium replacement rate of at least 25% daily replacement for more than one day (see Claim 38). Therefore, the present claims cannot be anticipated by Freedman et al and therefore, withdrawal of this ground of rejection is requested.

The objections of Claim 9 and 43 are addressed by amendment.

The rejection of Claims 7-12, 38-45 and 47-48 under 35 U.S.C. § 112, second paragraph is addressed by amendment. Claim 38 is amended to clarify that the lineage committed cells are those cells that are differentiated to at least a point where they are programmed to develop into a specific type of cell (see also page 6, lines 18-20).

The rejection of Claims 7-12, 38-45 and 47 under 35 U.S.C. § 112, first paragraph is addressed by amendment. Claim 38 is amended to clarify that the lineage committed cells cultured are lineage committed hematopoietic cells, which is described and enabled by the specification on page 7, lines 14-18 and lines 20-22); pages 12-19; and the Examples. Therefore, withdrawal of this rejection is requested.

Concerning the comment raised by the Examiner in the Advisory Action (page 2 of paper no. 34, Continuation of 2), Claim 38 is directed to culturing human lineage committed cell compositions, which cells are programmed to develop into a specific type of cell. The biological function which is enhanced by the culturing procedure is described in the application on page 10, last paragraph. The culturing method facilitates obtaining cells with the enhanced biological function, again which is enhanced relative to cells cultured in static culture (see page 5, 2nd paragraph of the specification). In an attempt to clear up the Examiner's confusion, the phrase defining the cell differentiation has been moved from the last clause of Claim 38 to the portion of the claim where the lineage committed cell composition is first noted in the method. If the Examiner requires further clarification on this or any other issue in this application he is invited to contact the Applicants' undersigned representative to resolve the matter expediently.

Applicants submit the present application is now ready for allowance. Early notification of such allowance is earnestly solicited.

Respectfully submitted,

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